

CLAIMS

1. A monoclonal antibody that specifically binds transthyretin comprising three heavy chain CDRs and three light chain CDRs of SEQ ID NOS. 1 and 13 respectively.
2. The antibody of claim 1 comprising three Kabat heavy chain CDRs designated SEQ ID NOS: 10-12, respectively and three light CDRs designated SEQ ID NOS: 18-20, respectively.
3. The antibody of claim 1, wherein the sequence of heavy chain CDR-H1 is SEQ ID NO: 63.
4. The antibody of claim 1 that is a chimeric, humanized, or veneered antibody.
5. The antibody of claim 1, wherein the antibody is a human IgG1 isotype.
6. The antibody of claim 1 wherein the antibody has a human IgG2 or IgG4 isotype.
7. The antibody of claim 1, that is a humanized or chimeric antibody.
8. The humanized antibody of claim 7 comprising a humanized mature heavy chain variable region having an amino acid sequence at least 90% identical to SEQ ID NO:9 and a humanized mature light chain variable region having an amino acid sequence at least 90% identical to SEQ ID NO:17.
9. The humanized antibody of claim 8, provided position H77 is occupied by T.
10. The humanized antibody of claim 9, provided position H49 is occupied by A.
11. The humanized antibody of claim 9, provided positions H19, H44, H83, and H89 are occupied by K, R, K, and M, respectively.
12. The humanized antibody of claim 11, provided position H49 is occupied by A.
13. The humanized antibody of claim 9, provided position L45 is occupied by K.

14. The humanized antibody of claim 8, comprising a mature heavy chain variable region having an amino acid sequence at least 95% identical to SEQ ID NO:9 and a mature light chain variable region having an amino acid sequence at least 95% identical to SEQ ID NO:17.

15. The humanized antibody of claim 14, comprising a mature heavy chain variable region having an amino acid sequence at least 98% identical to SEQ ID NO:9 and a mature light chain variable region having an amino acid sequence at least 98% identical to SEQ ID NO:17.

16. The humanized antibody of claim 9, wherein the mature heavy chain variable region has the amino acid sequence of SEQ ID NO: 9.

17. The humanized antibody of claim 16, wherein the mature light chain variable region has the amino acid sequence of SEQ ID NO: 17.

18. The antibody of claim 1, wherein the antibody is an intact antibody.

19. The antibody of claim 1, wherein the antibody is a binding fragment.

20. The antibody of claim 19, wherein the binding fragment is a single-chain antibody, Fab, or Fab'2 fragment.

21. The humanized antibody of claim 8, wherein the mature light chain variable region is fused to a light chain constant region and the mature heavy chain variable region is fused to a heavy chain constant region.

22. The humanized antibody of claim 21, wherein the heavy chain constant region is a mutant form of a natural human heavy chain constant region which has reduced binding to a Fc.gamma. receptor relative to the natural human heavy chain constant region.

23. The humanized antibody of claim 21, wherein the heavy chain constant region is of IgG1 isotype.

24. The humanized antibody of claim 21, wherein the mature heavy chain variable region is fused to a heavy chain constant region having the sequence of SEQ ID NO:26 and/or

the mature light chain variable region is fused to a light chain constant region having the sequence of SEQ ID NO:28.

25. The humanized antibody of claim 21, wherein the mature heavy chain variable region is fused to a heavy chain constant region having the sequence of SEQ ID NO:26 with or without the C-terminal lysine and/or the mature light chain variable region is fused to a light chain constant region having the sequence of SEQ ID NO:28.

26. A pharmaceutical composition comprising the antibody of claim 1 and a pharmaceutically acceptable carrier.

27. A nucleic acid or nucleic acids encoding the heavy chain and light chain of the antibody of claim 1.

28. A recombinant expression vector comprising the nucleic acid of claim 27.

29. A host cell transformed with the recombinant expression vector of claim 28.

30. A method of humanizing an antibody, the method comprising: (a) selecting an acceptor antibody; (b) identifying the amino acid residues of the mouse antibody to be retained; (c) synthesizing a nucleic acid encoding a humanized heavy chain comprising CDRs of the mouse antibody heavy chain and a nucleic acid encoding a humanized light chain comprising CDRs of the mouse antibody light chain; and (d) expressing the nucleic acids in a host cell to produce a humanized antibody; wherein the mouse antibody comprises a heavy chain variable region having the amino acid sequence of SEQ ID NO:1 and a light chain variable region having the amino acid sequence of SEQ ID NO:13.

31. A method of producing a humanized, chimeric, or veneered antibody, the method comprising: (a) culturing cells transformed with nucleic acids encoding the heavy and light chains of the antibody, so that the cells secrete the antibody; and (b) purifying the antibody from cell culture media; wherein the antibody is a humanized, chimeric, or veneered form of the antibody of claim 1.

32. A method of producing a cell line producing a humanized, chimeric, or veneered antibody, the method comprising: (a) introducing a vector encoding heavy and light

chains of an antibody and a selectable marker into cells; (b) propagating the cells under conditions to select for cells having increased copy number of the vector; (c) isolating single cells from the selected cells; and (d) banking cells cloned from a single cell selected based on yield of antibody; wherein the antibody is a humanized, chimeric, or veneered form of the antibody of claim 1.

33. Use of the antibody of claim 1 in the manufacture of a medicament for inhibiting or reducing aggregation of transthyretin in a subject having or at risk of developing a transthyretin-mediated amyloidosis.

34. Use of the antibody of claim 1 in the manufacture of a medicament for inhibiting or reducing transthyretin fibril formation in a subject having or at risk of developing a transthyretin-mediated amyloidosis.

35. Use of the antibody of claim 1 in the manufacture of a medicament for reducing transthyretin deposits in a subject having or at risk of developing a transthyretin-mediated amyloidosis.

36. Use of the antibody of claim 1 in the manufacture of a medicament for clearing aggregated transthyretin in a subject having or at risk of developing a transthyretin-mediated amyloidosis, wherein the medicament is to be administered to the subject to thereby clearing aggregated transthyretin from the subject relative to a subject having or at risk of developing a transthyretin-mediated amyloidosis who has not received the antibody.

37. The use of any one of claims 33 to 36, wherein the transthyretin-mediated amyloidosis is selected from the group consisting of senile systemic amyloidosis (SSA), senile cardiac amyloidosis (SCA), familial amyloid polyneuropathy (FAP), familial amyloid cardiomyopathy (FAC), and central nervous system selective amyloidosis (CNSA).

38. The antibody of any one of claims 1 to 25 for use in a therapy.

39. An *in vitro* method of detecting the presence or absence of transthyretin deposits in a subject, comprising contacting a biological sample obtained from the subject suspected of comprising the amyloid accumulation with an effective amount of the antibody of claim 1.